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VIP Oxidative Carbonylation

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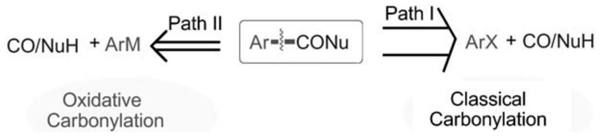
Palladium-Catalyzed Aerobic Oxidative Carbonylation of Arylboronate Esters under Mild Conditions**

*Qiang Liu, Gang Li, Jun He, Jing Liu, Peng Li, and Aiwen Lei**

The transition-metal-catalyzed carbonylation involving CO gas is a fundamental chemical transformation, which not only extends the carbon chain length, but also introduces a synthetically versatile carbonyl group. Theoretically, as shown in Scheme 1, the Ar group could originate from an electrophile (ArX; Path I) or a nucleophile (ArM; Path II). The carbonylation of organic halides (ArX) with CO, pioneered by Heck and co-workers,[1a] has attracted broad interest in the past 40 years, and is widely applied to the synthesis of fine chemicals in industry.[1–3] In the reaction systems shown in Scheme 1, the π-acceptor property of CO renders low-valent metal catalysts such as Pd^0 species to be relatively electron deficient, and makes the oxidative addition of organic halides towards Pd^0 species difficult.[4] Consequently, the reaction in Path I usually requires relatively harsh conditions; for example, high temperatures or high CO pressures.[5,6]



Scheme 1. Two theoretical aryl carbonylation pathways (ArM; M = H, In).

Recently, oxidative carbonylation of ArM (M = H, In) with CO has emerged as a conceptually new alternative to “classic carbonylation processes”.[7–11] The use of CO avoids the reluctant oxidative addition step, which is mentioned above in traditional carbonylations, and has the potential to accommodate milder reaction conditions. The oxidative carbonylation of ArH shows promise when catalyzed by transition metals, whereas the current transformation usually requires the use of directing groups.[7–10] Furthermore, the oxidative carbonylation of arylindium derivatives requires the use of stoichiometric amounts of the oxidant desyl chloride.[11] Herein, we report the first example of the oxidative carbonylation of arylboronic acid derivatives under balloon pressure of CO with air as the oxidant at 40→50 °C.

Arylboronic acid derivatives are air and moisture stable, and are compatible with a broad range of common functional groups.[12–14] For these reasons, they have been widely applied in chemical syntheses.[15–17] Recently, the research groups of Hou[18] and Iwasawa[19] have reported a nucleophilic addition of arylboronate esters toward CO_2 in the presence of copper or rhodium catalysts, respectively. In the presence of CO, the Suzuki carbonylation reaction was also realized by Beller and co-workers, and resulted in the formation of biaryl ketones.[20] However, there is no literature precedent of their oxidative carbonylation to form carboxylate esters. Furthermore, with respect to cost and simplicity, air is the ideal oxidant for oxidative carbonylation.[21–26] The oxidative carbonylation of amines or alcohols was investigated by employing air or oxygen as the oxidant.[22,27–32] However, to the best of our knowledge, no example has been reported regarding the oxidative carbonylation of arylmetal reagents by employing oxygen or air as the sole oxidant.

To probe the feasibility of our proposed study, we chose the model substrates phenylBneop (**1a**; neop = $OCH_2C(CH_3)_2CH_2O$) and *n*-butanol to afford the carbonylation product **2a**, oxidative protodeboronation product **3a** and homocoupled product **4a**. Upon variation of the reaction conditions, different product distributions were observed (Table 1). Among the palladium catalysts used as precursors (Table 1, entries 1–11), $[PdCl_2(PPh_3)_2]$ showed the best result (56 % yield for **2a** and 44 % for **3a**; Table 1, entry 7), whereas the bidentate ligands gave poor results (Table 1, entries 1, 2, and 6). Interestingly, $Pd(OAc)_2/PPh_3$ (1:2) and $[Pd(dba)_2]/PPh_3$ (1:2) were not effective catalysts for this transformation (Table 1, entries 10 and 11). Using $[PdCl_2(MeCN)_2]/PPh_3$ (1:2) was equivalent to $[PdCl_2(PPh_3)_2]$, whereas $[PdCl_2(MeCN)_2]/PPh_3$ (1:4) was less effective at producing the carbonylation product **2a**, however, it was an efficient catalytic system for the oxidative homocoupling of **1a** (Table 1, entries 8 and 9).

Next, different bases were then studied (Table 1, entries 12–19). The results of triethylamine ($\mathbf{B^1}$) were similar to those of 2,2,6,6-tetramethylpiperidine ($\mathbf{B^2}$) and 2,6-lutidine ($\mathbf{B^3}$), however, other bases tested were less effective in this reaction. Furthermore, the ratio of air to CO was also screened. Interestingly, the yield of *n*-butyl benzoate (**2a**) improved with an increase in the ratio of air to CO (Table 1,

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[*] Q. Liu, G. Li, J. He, Dr. J. Liu, P. Li, Prof. A. Lei
The College of Chemistry and Molecular Sciences
Wuhan University, Wuhan, Hubei (China)
Fax: (+86) 27-6875-4067
E-mail: aiwenlei@whu.edu.cn
Homepage: http://www.chem.whu.edu.cn/GCI_WebSite/main.htm
Prof. A. Lei
State Key Laboratory for Oxo Synthesis and Selective Oxidation,
Lanzhou Institute of Chemical Physics
Chinese Academy of Sciences, 730000 Lanzhou (China)

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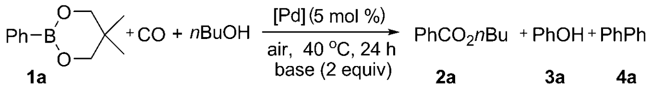
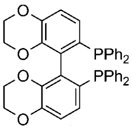
Table 1: Oxidative carbonylation of phenylboronate ester **1a**.[a]

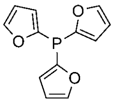


Entry	[Pd] Catalyst	Base	Air/CO	Yield [%][b]		
				2a	**3a**	**4a**
1	$Pd(OAc)_2/L^1$	Et_3N	1:3	21	46	0
2	$[PdCl_2(dppf)]$	Et_3N	1:3	0	0	0
3	$[PdCl_2(MeCN)_2]/L^2$ (1:2)	Et_3N	1:3	0	0	0
4	$[PdCl_2(MeCN)_2]/L^3$ (1:2)	Et_3N	1:3	0	0	0
5	$Pd(OAc)_2$/py (1:4)	Et_3N	1:3	0	0	0
6	$Pd(OAc)_2$/bpy	Et_3N	1:3	0	0	0
7	$[PdCl_2(PPh_3)_2]$	Et_3N	1:3	56	44	0
8	$[PdCl_2(MeCN)_2]/PPh_3$ (1:4)	Et_3N	1:3	0	12	80
9	$[PdCl_2(MeCN)_2]/PPh_3$ (1:2)	Et_3N	1:3	56	44	0
10	$Pd(OAc)_2/PPh_3$ (1:2)	Et_3N	1:3	26	34	0
11	$[Pd(dba)_2]/PPh_3$ (1:2)	Et_3N	1:3	0	0	0
12	$[PdCl_2(PPh_3)_2]$	*n*BuONa	1:3	32	68	0
13	$[PdCl_2(PPh_3)_2]$	CsF	1:3	32	67	0
14	$[PdCl_2(PPh_3)_2]$	K_3PO_4	1:3	45	53	0
15	$[PdCl_2(PPh_3)_2]$	dbu	1:3	47	50	0
16	$[PdCl_2(PPh_3)_2]$	dabco	1:3	0	0	0
17	$[PdCl_2(PPh_3)_2]$	B^1	1:3	51	47	0
18	$[PdCl_2(PPh_3)_2]$	B^2	1:3	54	42	0
19	$[PdCl_2(PPh_3)_2]$	B^3	1:3	54	38	0
20	$[PdCl_2(PPh_3)_2]$	Et_3N	1:10	43	30	0
21	$[PdCl_2(PPh_3)_2]$	Et_3N	1:5	47	36	0
22	$[PdCl_2(PPh_3)_2]$	Et_3N	1:1	58	40	0
23	$[PdCl_2(PPh_3)_2]$	Et_3N	3:1	75	24	0
24	$[PdCl_2(PPh_3)_2]$	Et_3N	5:1	74	24	0

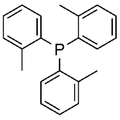
[a] Reaction conditions: Using **1a** (0.25 mmol), base (0.5 mmol), Pd catalyst (0.0125 mmol), and air/CO in 1 atm pressure. [b] Yield determined by GC analysis. bpy = 2,2′-bipyridine , dabco = 1,4-diazabicyclo-[2.2.2]octane, dbu = 1,8-diazabicyclo[5.4.0]undec-7-ene, dppf = diphenylphosphinoferrocene, py = pyridine.



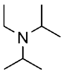
L^1



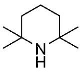
L^2



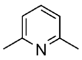
L^3



B^1

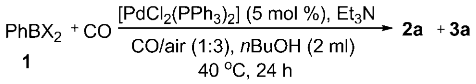


B^2



B^3

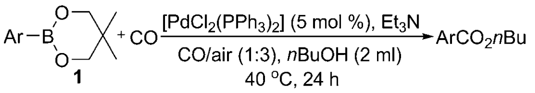
Table 2: Oxidative carbonylation of different arylboronic acid derivatives.[a]

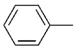
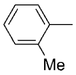
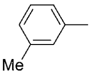
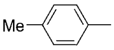
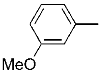
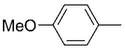
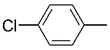
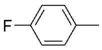
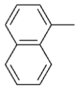
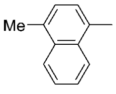


Entry	**1**	Yield [%][b]	
		2a	**3a**
1	$(PhBO)_3$	63	36
2	$PhB(OH)_2$	55	45
3	$PhBF_3K$	15	15

[a] Reaction conditions: Using **1** (0.25 mmol), Et_3N (0.5 mmol), $[PdCl_2(PPh_3)_2]$ (0.0125 mmol), CO/air (1:3) at 1 atm pressure. [b] Yield determined by GC analysis.

Table 3: Palladium-catalyzed aerobic oxidative carbonylation of ArBneop in *n*BuOH.[a]



Entry	**1**	Ar	Yield [%][b]
1	**1a**		75
2	**1b**		81
3	**1c**		85
4	**1d**		80
5	**1e**		79
6	**1f**		95
7	**1g**		66
8	**1h**		61
9	**1i**		74
10	**1j**		69

[a] Reaction Conditions: Using **1** (0.25 mmol), Et_3N (0.5 mmol), $[PdCl_2(PPh_3)_2]$ (0.0125 mmol), CO/air (1:3) at 1 atm pressure. [b] Yield of isolated product.

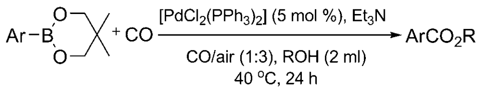
entries 20–24). Therefore, the optimized conditions for the oxidative carbonylation were 5 mol% of $[PdCl_2(PPh_3)_2]$ as the catalyst, triethylamine as the base, and a ratio of air/CO 3:1 at 40 °C.

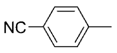
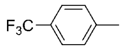
In Table 2, different arylboronic acid derivatives were compared under the optimized reaction conditions. The phenylboronic anhydride (63% yield of **2a**; Table 2, entry 1) performed slightly worse than **1a** (75% yield of **2a**; Table 1, entry 23). The oxidative carbonylation of phenylboronic acid produced **2a** in 55% yield (Table 2, entry 2). When potassium phenyltrifluoroborate was employed, the yields of both **2a** and **3a** were poor.

A further investigation of the substrate scope was carried out under the optimized reaction conditions. In Table 3, various ArBneop substrates were tested. Substrates containing electron-donating groups provided higher yields (Table 3, entries 1–6). The yields for *p*-MeO phenylBneop **1f** and *p*-fluoro phenylBneop **1h** are 95% and 61%, respectively (Table 3, entries 6 and 8). *Ortho*-substituted substrates, such as *o*-Me phenylBneop **1b** and naphthylBneop **1i** and **1j** gave satisfactory results (Table 3, entries 2, 9, and 10).

Furthermore, a variety of alcohols were tested and the results are listed in Table 4. In the presence of isopropanol, the reactions gave good results at 50 °C for 24 hours in the presence of 10 mol% of palladium catalyst (Table 4,

Table 4: Palladium-catalyzed aerobic oxidative carbonylation of ArBneop in different alcohols.[a]

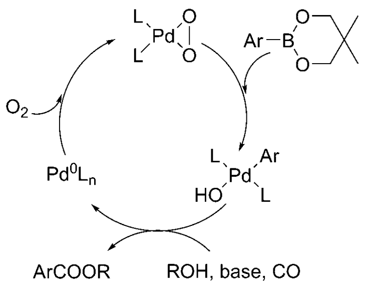


Entry	**1**	Ar	Alcohol (ROH)	Yield [%][b]
1[c]	**1d**		*i*PrOH	78
2[c]	**1f**		*i*PrOH	75
3[c]	**1g**		*i*PrOH	70
4[c]	**1k**		*i*PrOH	85
5[c]	**1l**		*i*PrOH	71
6	**1e**		EtOH	77
7	**1i**		EtOH	70
8	**1a**		EtOH	73
9	**1f**		MeOH	90

[a] Reaction conditions: Using **1** (0.25 mmol), Et$_3$N (0.5 mmol), [PdCl$_2$(PPh$_3$)$_2$] (0.0125 mmol), and CO/air (1:3) at 1 atm pressure. [b] Yield of isolated product. [c] Used [PdCl$_2$(PPh$_3$)$_2$] (0.025 mmol) at 50 °C.

entries 1–5).[33] Ethanol and methanol worked well under the standard reaction conditions (Table 4, entries 6–9).

It is known that the reaction of [Pd(PPh$_3$)$_4$] with oxygen affords the [(η-O$_2$)Pd(PPh$_3$)$_2$] complex.[34] Jutand and coworkers investigated the transmetalation between the [(η-O$_2$)Pd(PPh$_3$)$_2$] complex and PhB(OH)$_2$, and a fast reaction generated the *trans*-[PhPd(OH)(PPh$_3$)$_2$] complex.[35,36] A proposed catalytic cycle of the aerobic oxidative carbonylation was shown in Scheme 2. Carbonylation of *trans*-[ArPd(OH)(PPh$_3$)$_2$] in the presence of CO, ROH, and base would result in the formation of product ArCOOR, and a Pd^{0}L$_n$ species. The [(η-O$_2$)Pd(PPh$_3$)$_2$] complex would be regenerated from the reaction of [Pd(PPh$_3$)$_n$] with air.

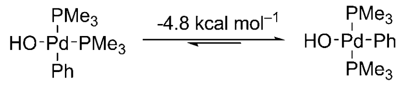


Scheme 2. Proposed mechanism.

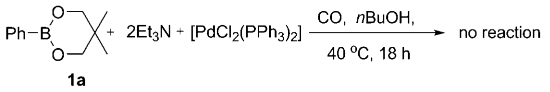
In Scheme 3, a simplified model was used to compare the energy difference between *cis*- and *trans*-[ArPd(OH)(L)$_2$]. The *trans* complex was 4.8 kcal mol^{-1} more stable than the *cis* complex. Thus, we speculated that in this oxidative carbonylation, *cis*-[ArPd(OH)(PPh$_3$)$_2$], initially produced from the transmetalation of [(η-O$_2$)Pd(PPh$_3$)$_2$] with PhB(OH)$_2$, would quickly transform into *trans*-[ArPd(OH)(PPh$_3$)$_2$].

In the presence of CO gas, two experiments revealed the different transmetalation reactivities of [PdCl$_2$(PPh$_3$)$_2$] and [(η-O$_2$)Pd(PPh$_3$)$_2$] complex with **1a**. No biphenyl or any carbonylation products were identified in the reaction of **1a** with a stoichiometric amount of [PdCl$_2$(PPh$_3$)$_2$] when NEt$_3$ was employed as the base [Eq. (1)]. In fact, starting material **1a** was quantitatively recovered. However, when [PdCl$_2$(PPh$_3$)$_2$] was replaced by a stoichiometric amount of [(η-O$_2$)Pd(PPh$_3$)$_2$], *n*-butyl benzoate (**2a**) and phenol (**3a**) were obtained in 50 % yield, respectively [Eq. (2)]. Similarly, in the absence of CO and air at 40 °C using NEt$_3$ as the base and *n*BuOH as the solvent, **1a** did not react with a stoichiometric amount of [PdCl$_2$(PPh$_3$)$_2$] either [Eq. (3)]. However, in air, the homocoupled product biphenyl (**4a**) and oxidative protodeboronation product phenol (**3a**) were generated in 56 % and 44 % yield, respectively [Eq. (4)]. These comparative results indicated that the transmetalation reaction could only occur between phenylBneop and [(η-O$_2$)Pd(PPh$_3$)$_2$] under these reaction conditions; [PdCl$_2$(PPh$_3$)$_2$] as the catalyst precursor needs to convert into [(η-O$_2$)Pd(PPh$_3$)$_2$] before initiating the catalytic cycle.

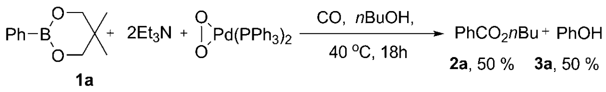
To study whether peroxide species were formed in this reaction, aliquots were tested using potassium iodide starch. Interesting, the test paper did not turn blue in the early stage of the reaction (the solution of the reaction was yellow). When the yellow reaction solution turned red, the potassium iodide starch test paper turned blue, thus proving that the peroxides were formed during the reaction.



Scheme 3. The Gibbs free energy difference between *cis*- and *trans*-[ArPd(OH)(L)$_2$].



(1)



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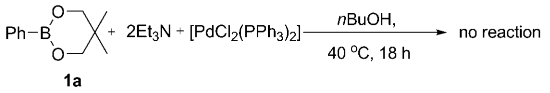

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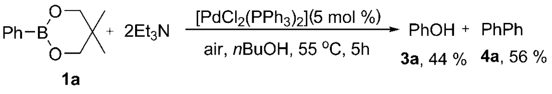

(4)

Another interesting finding is that there was almost no biaryl product formed in this oxidative carbonylation. However, arylboronic acid derivatives could be homocoupled in the presence of oxygen.[37–39] The difference between the oxidative homocoupling and this oxidative carbonylation was mainly attributed to the presence or absence of CO. Thus, we presumed that it was CO which led the high selectivities between the oxidative carbonylation and oxidative homocoupling, but we do not have enough data to confirm this at present.

In conclusion, we have developed a novel oxidative carbonylation reaction. Under a balloon pressure of CO/air and at temperatures of 40→50 °C, readily available arylboronic acid derivatives could be converted into their corresponding carbonylative products using $[PdCl_2(PPh_3)_2]$ as the catalyst precursor. It is the first example whereby arylboronic acid derivatives can be transformed into carbonylative products using air as the sole oxidant under mild conditions.[34]

Experimental Section

General procedure: $[PdCl_2(PPh_3)_2]$ (0.0125 mmol) and arylboronate ester (0.25 mmol) was added to a Schlenk tube equipped with a stirrer bar. A balloon filled with air and CO (the ratio is 3:1) was connected to the Schlenk tube through the side arm. The mixture was purged with the mixed gas for 1 min before triethylamine (0.5 mmol) and 1-butanol (2 mL) were added. The Schlenk tube was placed in an oil bath and heated to 40 °C for 24 h, and then cooled to room temperature. After the crude mixture was concentrated under vacuum, the reaction mixture was purified by flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate 60:1) to afford the product.

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Keywords: air oxidation · arylboronate esters · homogeneous catalysis · oxidative carbonylation · palladium

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